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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/782,816	02/14/2001	David J. Sharp	UC069.001A	1726

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EXAMINER	
YAEN, CHRISTOPHER H	
ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 02/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/782,816	SHARP ET AL.	
	Examiner	Art Unit	
	Christopher H. Yaen	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 May 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,9-11,15,17,21 and 22* is/are pending in the application.

4a) Of the above claim(s) *3* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,9-11,15,17,21 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 February 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/25/01 & 10/18/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Exhibits 1-4*.

DETAILED ACTION

Re: Sharp *et al*

Election/Restrictions

1. Applicant's election with traverse of group I (claims 1-3, 9-11, 15,17, and 21-22) in the reply filed on 5/21/2003 is acknowledged. The traversal is on the ground(s) that the search for the different inventions is not burdensome and that the inventions ca be searched together. In particular, applicant argues that the claimed sequence all share a "common chemical structure" and "common function". Moreover, applicant contends that the search for the different inventions would not be burdensome given the fact that the peptides are used for the same or similar purposes. In addition, applicant argues that there would be considerable burden on the applicant if the claimed inventions is separated into distinct inventions. This is not found persuasive because applicant has already canceled claims or parts of claims that are drawn to separate and distinct inventions. In addition, the search for the different sequences would in fact be burdensome to search together. In particular, the search for the different sequences would require the analysis of at least 50 different sequences all of which are not related in structure because each permutation of the sequences, by definition, would create a different and distinct sequence. As such, the search for the different sequences as originally claimed would be burdensome.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 4-8,12-14,16,18-20, and 23-27 are canceled without prejudice or disclaimer.

3. Claims 1-3,9-11,15,17, and 21-22 are pending. Claim 3 is withdrawn from further consideration as being drawn to a non-elected invention because applicant has elected SEQ ID No: 1 for prosecution on the merits. It appears that claim 3 is drawn to a peptide derived from SEQ ID No: 2.

4. Claims 1-2, 9-11,15, 17, and 21-22 are examined on the merits.

Information Disclosure Statement

5. The Information Disclosure Statements filed 6/25/01 and 10/18/2002 are acknowledged and considered. Signed copies of the IDSs are attached hereto.

Claim Rejections - 35 USC § 112, 2nd paragraph

6. Claims 1,2,9-11,15,17, and 21-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites, "m" following the "$(X1)_n$EVEKIKTTVKESATEEKLTPVX2L(X3)" motif. The term has not be defined in the specification. For examination purposes, the claim will be interpreted without the "m".

Claim Rejections - 35 USC § 112, 1st paragraph

7. Claims 11, 17, and 21-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated protein comprising the motif of "$(\mathbf{X1})_n$EVEKIKTTVKESATEEKLTPV**X2**L(**X3**) capable of modulating cellular

proliferation or inhibiting cellular proliferation and a method of inhibiting cellular proliferation comprising the delivering to a target cell the said isolated peptide, does not reasonably provide enablement for a peptide capable of "selectively inhibiting cancerous cells" or for a method of inhibiting cellular proliferation comprising delivering a nucleic acid encoding said protein . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). Wands states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The claims are drawn to an isolated peptide with the motif of "(**X1**)$_n$EVEKIKTTVKESATEEKLTPV**X2**L(**X3**) and a method of inhibiting cellular proliferation of comprising the delivery of a peptide or nucleci acid encoding said peptide to a target cell. The invention is in a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." *Mycogen Plant Sci., Inc. v. Monsanto Co.*, 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The breadth of the claims

The claims as interpreted read on peptides capable of selectively targeting and treating cancerous cells only without affecting non-cancerous cells as well as a method of involving gene thereapy.

The unpredictability of the art and the state of the prior art

The treatment of cancer in general is at most unpredictable, as underscored by Gura (Science, v278, 1997, pp.1041-1042) who discusses the potential shortcomings of potential anti-cancer agents including extrapolating from in-vitro to in-vivo protocols, the problems of drug testing in knockout mice, and problems associated with clonogenic assays. Indeed, since formal screening began in 1955, thousands of drugs have shown activity in either cell or animal models, but only 39 that are used exclusively for chemotherapy, as opposed to supportive care, have won approval from the FDA (page 1041, 1st column) wherein the fundamental problem in drug discovery for cancer is that the model systems are not predictive. Moreover, the specification of the instant application teaches that one of the major assumptions for the instant invention is its ability to inhibit the ability of dynein to bind without perturbing its function elsewhere in the cell. Thus it is unclear whether the instant peptide is capable of "selectively" inhibiting a cancerous cell as claimed.

With regards to method claims reading on gene therapy, at the time the application was filed, the art of administering any type of genetic expression vector to an individual so as to provide a tangible therapeutic benefit was poorly developed and unpredictable. The NIH ad hoc committee to assess the current status and promise of

gene therapy reported in December 1995 that "clinical efficacy has not been definitively demonstrated at this time in any gene therapy protocol, despite anecdotal claims...," and that "significant problems remain in all basic aspects of gene therapy" (Orkin and Motulsky, p. 1). In a review article published in Scientific American in June 1997, Theodore Friedmann discusses the technical barriers which have so far prevented successful gene therapy, and states "So far, however, no approach has definitively improved the health of a single one of the more than 2,000 patients who have enrolled in gene therapy trials worldwide" (p. 96). In a review article published in Nature in September 1997, Inder Verma states "Although more than 200 clinical trials are currently underway worldwide, with hundreds of patients enrolled, there is still no single outcome that we can point to as a success story" (p. 239).

In an article published well after the effective filing date of the instant application, Rubanyi (2001) teaches that the problems described above remain unsolved at the time the instant application was filed. Rubanyi states, "[a]lthough the theoretical advantages of [human gene therapy] are undisputable, so far [human gene therapy] has not delivered the promised results: convincing clinical efficacy could not be demonstrated yet in most of the trials conducted so far ..." (page 113, paragraph 1). Among the technical hurdles that Rubanyi teaches remain to be overcome are problems with gene delivery vectors and improvement in gene expression control systems (see especially the section under "3. Technical hurdles to be overcome in the future", pp. 116-125).

The state of the art is such that no correlation exists between successful expression of a gene and a therapeutic result (Ross et al., p. 1789, column 1, paragraph 1).

All of this underscores the criticality of providing workable examples which is not disclosed in the specification, particularly in an unpredictable art, such as cancer therapy.

Working examples

The specification provides an example of microinjecting peptides into a *Drosophila* embryo model (see page 27-29, for example).

Guidance in the specification

No guidance has been provided in the specification with regard to a peptide that is capable of "selectively" target cancerous cells or a method of gene therapy.

Level of skill in the art

The level of skill in the art is deemed to be high.

Conclusion

Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that ad, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the presence of a working example which does not address the issue of the efficacy of the control and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Claim Rejections - 35 USC § 112, 1st paragraph

8. Claims 1,9-11, 17, and 21-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case has only set forth a peptide sequence comprising the motif of "(**X1**)$_n$EVEKIKTTVKESATEEKLTPV**X2**L(**X3**) and SEQ ID No: 51, and therefore the written description is not commensurate in scope to the claims that read on peptides that are "fragments or derivatives having at least 90% identify with SEQ ID No: 1 as claimed. The following *written description* rejection is set forth herein.

The claims recite a "fragment" "derivatives" having at least about 90% indeitify to SEQ ID No: 1 as part of the invention. However, there does not appear to be an adequate written description in the specification as-filed of the essential structural feature that provides the function of modulating or inhibiting cellular proliferation. The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying

characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

Applicant does not appear to have reduced to practice fragments or derivatives or any sequence having at least 90% identify to SEQ ID No: 1, as claimed. Neither has Applicant provided a sufficient written description of any structure that may be correlated with the desired modulatory function. Applicant has not provided a sufficient representative number of species to show possession of the broad genus of fragments, derivatives or homologues claimed. Thus the genus of peptides encompassed by this term is extensive and the artisan would not be able to recognize that Applicant was in possession of the invention as now claimed.

Consequently, Applicant was not in possession of the instant claimed invention. See Regents of the University of California v. Eli Lilly and Co. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). Adequate written description of genetic material "'requires a precise definition, such as by structure, formula, chemical name, or physical properties,' not a mere wish or plan for obtaining the claimed chemical invention." Id. 43 USPQ2d at 1404 (quoting Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606). The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter of the claim. Id. 43 USPQ2d at 1406. A description of what the genetic material does, rather than of what it is, does not suffice. Id.

While it is noted that the instant claims are drawn to methods, the claims nevertheless require an adequate written description of the "fragments" or "derivatives" having at least 90$ identify employed in the methods.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001. Applicant is invited to point to clear support or specific examples of the claimed invention in the specification as-filed.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

10. Claims 1,2,9,10,11, 15,17,21 and 22 are rejected under 35 U.S.C. 102(a) as being anticipated by Rosen *et al* (WO 00/55173). Rosen *et al* teach a isolated peptide comprising the motif of "(**X1**)$_n$EVEKIKTTVKESATEEKLTPV**X2**L(**X3**), wherein "n" = 0, and X2 = L, and X3 = SEQ ID No: 22 (see page 646-648 of the sequence listing and attached sequence alignment - Exhibit 1). For the purposes of this rejection, the term "is" as recited in claim 2 is interpreted as being open language or "comprising" language, therefore, Rosen *et al* also teach a peptide comprising SEQ ID No: 51 (see attached sequence alignment - Exhibit 2) as well as peptides comprising pharmaceutical carriers. Rosen *et al* also teach methods of using the claimed peptide

for the treatment of disorders including cancer (see for example page 3). Although the reference does not specifically teach that the isolated peptide induces is capable of modulating or inhibiting cellular proliferation, selectively inhibiting cancerous cells, the claims are drawn to the product *per se* and inherently, such a peptide would modulate or inhibit cellular proliferation or selectively inhibit cancerous cells. Thus, the claimed peptide appears to be the same as the prior art. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1,2, and 9-11 are rejected under 35 U.S.C. 102(b) as being anticiapted by Echeverri C.J. *et al* (J. Cell Biol. 1996; 132:617-633, IDS 6/25/2001 #10). Echeverri *et al* teach an isolated protein comprising a (**X1**)$_n$EVEKIKTTVKESATEEKLTPV**X2** L(**X3**) motif, wherein "n" = 0, and X2 = L, and X3 = SEQ ID No: 22 as claimed (see page 620,

for example, also see attached sequence alignment exhibit 3). For the purposes of this rejection, the term "is" as recited in claim 2 is interepreted as being open language or "comprising" language. Thus, Echeverri *et al* also teach a peptide comprising SEQ ID No: 51 (see attached sequence alignment - exhibit 4). Although the reference does not specifically teach that the isolated peptide induces is capable of modulating or inhibiting cellular proliferation, selectively inhibiting cancerous cells, the claims are drawn to the product *per se* and inherently, such a peptide would modulate or inhibit cellular proliferation or selectively inhibit cancerous cells. Thus, the claimed peptide appears to be the same as the prior art. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H. Yaen whose telephone number is 571-272-0838. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Christopher Yaen, Examiner
Art Unit 1643
February 3, 2006

CHRISTOPHER YAEN
PATENT EXAMINER